Researchers make a case for free fatty acids

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The current global epidemic of obesity-linked diabetes and its associated consequences -cardiovascular, neurological and renal diseases - is a growing public health problem for which therapeutic options are limited.

In obesity, fatty acids, derived mostly from adipose tissue, alter lipid metabolism in other tissues such as liver and skeletal muscles. Both impaired fatty acid metabolism and glucose are hallmarks of diabetes.

In a recent study in the journal *Biochemistry*, a research group led by James A. Hamilton, PhD, professor of physiology, biophysics and radiology at Boston University School of Medicine (BUSM), applied novel fluorescent methods to measure the rate by which fatty acids bind to and move across the fatty acid membrane to become metabolized.

"Our study shows that fatty acid entry into cells occurs by diffusion without catalysis by a protein previously described as a fatty acid transport protein. However, this protein promotes intracellular metabolism and storage," said Hamilton. "With this advance in basic science, new drugs can be designed that target the exact mechanism more precisely than currently available drugs."

Previous research has shown that glucose transport under the control of insulin is mediated by a transport protein called GLUT4. However, how fatty acids enter into cells has been an important unsolved problem, especially whether there are gatekeeper plasma membrane proteins that regulate fatty acid translocation across the membrane, thereby controlling the supply of fatty acids to the interior of the cell. Although

several proteins postulated to be fatty acid transporters have now been shown to have other roles, the mechanistic roles of the protein CD36 have remained elusive and are widely debated.

After measuring the products of fatty acid metabolism over time, the researchers found that CD36 enhances fatty acid metabolism into triglycerides (fat deposits), without increasing fatty acid translocation across the membrane in a cell line that does not normally synthesize triglycerides. Thus, CD36 increases fatty acid uptake by increasing intracellular metabolism, which promotes diffusion of fatty acids into cells.

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